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Combining Predictive Capabilities of Transcranial Doppler with Electrocardiogram to Predict Hemorrhagic Shock

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Abstract— **Hemorrhagic shock (HS) potentially impacts the chance of survival in most traumatic injuries. Thus, it is highly desirable to maximize the survival rate in cases of blood loss by predicting the occurrence of hemorrhagic shock with biomedical signals. Since analyzing one physiological signal may not enough to accurately predict blood loss severity, two types of physiological signals - Electrocardiography (ECG) and Transcranial Doppler (TCD) - are used to discover the degree of severity. In this study, these degrees are classified as mild, moderate and severe, and also severe and non-severe. The data for this study were generated using the human simulated model of hemorrhage, which is called lower body negative pressure (LBNP). The analysis is done by applying discrete wavelet transformation (DWT). The wavelet-based features are defined using the detail and approximate coefficients and machine learning algorithms are used for classification. The objective of this study is to evaluate the improvement when analyzing ECG and TCD physiological signals together to classify the severity of blood loss. The results of this study show a prediction accuracy of 85.9% achieved by support vector machine in identifying severe/non-severe states.**

I. Introduction

HEMORRHAGE is the most severe factor in traumatic injuries and their critical care. Since hemorrhage can cause inadequate tissue perfusion and organ damage, a condition termed hemorrhage shock (HS) relies heavily on the early diagnosis and treatment [1, 2]. Classifying the degree of severity of blood loss is vital in ensuring prompt treatment and a higher survival rate. Prompt detection and treatment of hemorrhagic injuries is also essential in the military field and for civilian trauma patients. Therefore, it is highly desirable to evaluate the severity of blood loss and predict the future occurrence of hemorrhagic shock (HS) by processing biomedical signals available in clinical settings.

Biological time series recognition analysis has been studied for many years to obtain significant information associated with diseases. For example, Electrocardiography (ECG) analysis has been shown to provide abnormal heart function information about autonomic control of the cardiovascular system, and so can explain a variety of cardiac dysfunctions [3]. By analyzing the physiological signal, an early diagnosis may be obtained. Even though, ECG combined with blood pressure (BP) is useful for analyzing cardiac activity, it may be insufficient for early estimation of hemorrhagic shock [4, 5, 6]. Incorporating other physiological signals may therefore further improve such estimations.

Transcranial Doppler (TCD) ultrasound is a non-invasive medical monitoring method that is clinically used to examine the circulation of blood inside the human brain. During typical TCD monitoring, ultrasound waves, which are transmitted through the tissues inside the skull, are reflected by the red blood cells moving along the blood vessels. Detection of these echoes allows estimation of blood flow. The real-time use of TCD monitoring can also be used to observe and record the blood flow inside the brain during a number of important surgical procedures [14, 15]. Therefore, in this study multiple physiological signals such as ECG and TCD signals are used and compared for their ability to further improve estimation of blood loss severity.

Many physiological time series are non-stationary, as they show very irregular and complex time-varying statistical patterns. Simple statistics based on mean and standard deviation quantitative analysis of physiological signals is used to provide knowledge of physiological significance. However, standard deviation alone may not provide an appropriate characterization of the rapid changes in a physiological system. For the purpose of characterizing fluctuation of the signal, power spectral density (PSD) [3, 19] is commonly used. PSD depends on techniques that provide information on the frequency components present in the signal. However, it does not provide the locality of these frequency changing contents. Because of this limitation, PSD may not appropriate to analyze non-stationary signals; a

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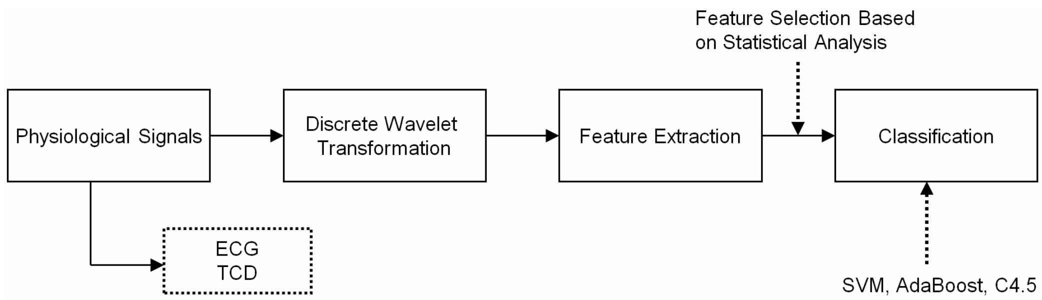

Fig. 1. A schematic diagram for the entire process.

challenge, considering that most physiological signals are non-stationary.

In order to overcome those disadvantages, time-frequency analysis based on wavelet transformation has been utilized [16] for this study. Since wavelet transformation provides desirable characteristics in time-frequency signal processing [8, 11], it is suitable for analyzing the time-varying characteristics of non-stationary signals such as ECG.

The objective of this study was to classify the severity of hemorrhage from patterns in physiological signals using discrete wavelet transformation (DWT) and machine learning. The performance of the wavelet method was tested using multiple physiological signals such as ECG and TCD signals from a model of hemorrhage in healthy conscious humans, called lower body negative pressure (LBNP). Machine learning (ML) algorithms were then applied to predict hemorrhage states i.e., mild, moderate and severe, and non severe and severe.

LBNP has proven to be a useful tool for simulating the early phase of hemorrhage in humans [12]. As such, this study uses physiological data generated from LBNP experiments.

II. Methods

A. Description of Dataset

Lower body negative pressure (LBNP) is widely used as a human demonstration model for studying acute hemorrhage analysis. A previous study [17] states that LBNP is a useful model to simulate acute hemorrhage in humans, since both induce similar physiological responses. Comparisons between physiological responses to LBNP and blood loss have demonstrated that some amount of blood loss and LBNP cause similar physiological reactions.

The LBNP dataset is comprised of forty subjects and was provided by the U.S. Army Institute of Surgical Research (USAISR) under a protocol approved by the Institutional Review Boards of both the USAISR and Virginia Commonwealth University.

Each test subject's lower body was placed inside the LBNP chamber and sealed at the iliac crest. The LBNP protocol consisted of a 5-min rest period (0 mm Hg) followed by 5 min of chamber decompression to -15, -30, -45, and -60 mm Hg and additional increments of -10 mm Hg every 5 minutes until the onset of cardiovascular collapse defined by one or a combination of the following criteria: a) a precipitous decrease in systolic blood pressure (SBP) (> 15 mm Hg); b) a sudden decrease in pulse rate (> 15 beats/min); progressive diminution of SBP < 70 mm Hg; and/or d) voluntary subject termination due to onset of pre-syncopal symptoms such as gray-out, sweating, nausea, or dizziness. Continuous ECG was recorded. Beat-by-beat systolic (SBP) and diastolic (DBP) blood pressures were measured non-invasively using an infrared finger photoplethysmograph (Finometer® Blood Pressure Monitor, TNO-TPD Biomedical Instrumentation, Amsterdam, The Netherlands). Also, a real measure of cerebral blood flow signal, TCD, was recorded.

The electrical signals used in our dataset were both sampled at 500 per second (i.e., 500Hz). In order to aid understanding of the data analysis process, the overall procedure is described in Figure 1.

B. Discrete Wavelet Transformation (DWT)

This section describes the pre-processing procedure, including signal segmentation and filtering, as well as DWT analysis. First, each physiological signal is segmented based on the LBNP stages (i.e., 5-min stages) to divide stages from baseline to collapse. Filtering is then applied to remove unwanted frequencies. In order to remove a specific frequency associated with power line (60 Hz), a notch filter centered at this frequency is employed [13], and then a band-pass filter between 1Hz and 62 Hz is applied. The wavelet transform is suitable for analyzing non-stationary signals to extract time-frequency information from the signals with rapid fluctuation. For this study, discrete wavelet transformation (DWT) is directly applied to physiological signals. DWT decomposes a signal at different levels with different frequencies by calculating the correlations of the signal with a mother wavelet. A series of high pass filters is applied to the signal to analyze the high frequencies, and low pass filters are used to analyze the low frequencies [9, 11, 18]. Since there is no absolute way to choose a mother wavelet, the choice of the wavelet is heavily based on the shape of the signal itself. In this study, the Daubechies family is chosen considering their similarity to the physiological signal. In particular, level six of Daubechies 4 (db4) and level eight of db4 are tested for ECG and TCD signal. Detail and approximation coefficients are used for further analysis.

C. Feature Extraction

Once DWT is applied to the physiological signals, the effect of the coefficients from DWT among the stages, from baseline to collapse stage, is examined by measuring the sum of each coefficient to investigate whether the energy of each stage is significantly difference from the other level coefficients. Then the following features are calculated:

$$D^j = \frac{1}{n}\sum_{i=1}^{n}(d_i^j)^2,\ A = \frac{1}{n}\sum_{i=1}^{n}a_i^2$$

$$\varepsilon_l = -p\log_2 p,\ p = \frac{A}{D^1 + D^2 + D^3 + D^4 + A}, \quad (1)$$

where d_i^j is the detail coefficient at level j ($j = 1,2,\cdots,6$ and $j = 1,2,\cdots,8$), and a_i is the approximation coefficient. ε_l is relative entropy at approximation coefficient and D^j and A indicate energy at level j and approximation coefficient respectively. The coefficients are used to calculate the median of each level and approximation coefficient using a window size of twenty (κ_1^j); the point right before the median of each level and approximation coefficient using window size of twenty (κ_2^j); and the point right after median of each level and approximation coefficient using window size of twenty (κ_3^j).

For the TCD signal, the following features are calculated with level six and eight decomposition of DWT.

$$D^j = \sum_{i=1}^{n}(d_i^j)^2,\ \text{and } A = \sum_{i=1}^{n}(a_i)^2 \quad (2)$$

$$\varepsilon^j = -\sum p^j \log_2 p^j$$

$$v^j = \frac{1}{n}\sum_{j=1}^{n}(d_i^j - \mu^j)^2,\ \text{and } \mu^j = \frac{1}{n}(\sum_{i=1}^{n} d_i^j)$$

where p^j is calculated based on detail coefficient at each level j.

D. Classification using Machine learning (ML)

The task of classification using machine learning (ML) is to predict the severity class of any given case using a model with ten-fold cross validation. In this study, ML algorithms are used to generate a classification model to predict the LBNP severity based only on significant features. Three machine learning algorithms are tested and compared: Support Vector Machines (SVMs), AdaBoost, and C4.5. Each machine learning method is implemented using 10-fold cross validation.

In order to address the significance of using integrated physiological signals, two classifications are performed and compared: 1) using only features defined based on TCD signals, 2) using features defined based on ECG and TCD signals.

Each classification is performed to predict whether the condition is mild, moderate or severe, as well as severe or non-severe. Baseline information is not included in the classification task since this information cannot be known in civilian patients. Precision and recall were also calculated to validate the model.

III. RESULTS

This section first presents the results of ANOVA analysis in extracting the most significance features for prediction of blood loss severity. Then the results of classification are described.

When investigating the energy difference among the stages with the DWT coefficients, we found that ECG showed much energy difference at the approximation coefficient and a slight change of detail coefficient among the stages, from the baseline to collapse stage, using level six decompositions. For this study, only the approximation coefficient is used for further classification. The TCD signal showed significant change in detail coefficients rather than approximation coefficient when using level eight decompositions.

According to ANOVA analysis to obtain the most significant features to identify the severity of blood loss, relative entropy of ECG (p value <0.0001), energy of ECG (p value <0.0001), and right before median of ECG (p value < 0.0001) are significant. In addition, the sum of squares of level 1 of TCD (p value=0.0051), the sum of squares at level 7 of TCD (p value=0.0008), the sum of square at level 8 of TCD (p value <0.0001), entropy at level 5 of TCD (p value <0.0001), entropy at level 6 of TCD (p value <0.0001), entropy at level 8 of TCD (p value <0.0001), variance at level 6 of TCD (p value <0.0001), and variance at level 8 (p value <0.0001) are selected as significant features for TCD signal.

Table I and Table II show the classification results with two classes (severe and non-severe) and three classes (mild, moderate and severe). As SVM obtained the highest accuracy among the machine learning techniques, only the SVM results are presented here.

TABLE I
CLASSIFICATION RESULT WITH THREE CLASSES

	Accuracy	Avg. Precision	Avg. Recall
TCD only	70 %	67.4%	67.3%
ECG and TCD	75.5%	73.2%	73.3%

Table I presents the classification results using three classes. A total of 184 samples are used for classification: 60 samples for mild, 50 for moderate and 74 for severe. In addition, true positive (TP) of mild case was 55 out of 60 (91.6%), true positive of moderate cases was 26 out of 50 (52%) cases, and true positive of severe cases was 57 out of 74 (77%).

TABLE II
CLASSIFICATION RESULT WITH TWO CLASSES

	Accuracy	Avg. Precision	Avg. Recall
TCD only	84.2%	84.1%	82.9%
ECG and TCD	85.9%	85.8%	83.5%

Table II presents the classification results using two classes. For this classification, mild and moderate cases are combined as non-severe cases. A total of 183 samples are used: 110 non-severe and 74 severe. In addition, true positive (TP) of non-severe case was 100 out of 110 (90.9%) and true positive of severe cases was 55 out of 74 (74.3%) cases.

IV. DISCUSSION

This study identifies the severity of blood loss using wavelet based features that can help discover hidden underlying patterns in physiological signals. In addition, applying a multi-physiological signals approach improves the accuracy and reliability of the volume loss prediction with three classes (mild, moderate, and severe). In other words, analyzing ECG and TCD signals together provides slightly improved performance over the use of TCD alone when predicting blood loss severity. Also, this study shows that approximate coefficient of DWT with ECG which is described the correlation with very low frequency of the signal may express the valuable characteristic of hidden knowledge.

V. CONCLUSION

This study shows that the most accurate prediction of hemorrhage severity (mild, moderate, and severe/ severe and non-severe) can be achieved when ECG and TCD are used together rather than when TCD is used alone. The multi-physiological signal wavelet-based method is capable of promptly determining the degree of blood loss, which may provide a useful means for real-time remote triage and decision making.

As a continuation of this work, more physiological signals will be used to predict the severity of blood loss, and more features will be defined to extract hidden patterns via wavelet transformation.

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